AMENDMENTS

Amendments to the claims:

Please cancel claims 3, and 88-124, 127, 129-143, and 147 without prejudice or disclaimer, please amend claims 1, and 4-8 and please enter new claims 148 and 149 as set forth in the complete listing of the claims that follows. This complete listing of the claims replaces previous claim listings.

1. (Currently amended) A method for sequencing a target nucleic acid molecule, comprising~~consisting of~~ the steps of:

fragmenting the target nucleic acid molecule to produce a set of nucleic acid fragments each containing a sequence that corresponds to a sequence of the target nucleic acid;

hybridizing the set to an array of nucleic acid probes to form a target array of nucleic acid molecules, wherein:

each probe comprises a single-stranded portion comprising a variable region [[probes]]; and

the array comprises a collection of the probes with sufficient sequence diversity in the variable regions to hybridize all of the target sequence with complete or nearly complete discrimination;

releasing the nucleic acid fragments hybridized to the probes, thereby producing released fragments;

generating mass signals of the released fragments by mass spectrometry;

~~determining molecular weights of hybridized nucleic acids in the target array to identify hybridized probes; and~~

performing a comparison of the mass signals to known reference mass signals; and

based upon the mass signals after the comparison ~~identified hybridized probes~~, determining the sequence of the target nucleic acid.

2. (Previously presented) The method of claim 1, wherein the molecular weights are determined by a method selected from the group consisting of gel electrophoresis, capillary electrophoresis, chromatography, and nuclear magnetic resonance.

3. (Cancelled).

4. (Currently amended) The method of claim [[3]] 1, wherein the mass spectrometry comprises a step selected from the group consisting of laser heating, droplet release, electrical release, photochemical release, fast atom bombardment, plasma desorption, matrix-assisted laser desorption/ionization, electrospray, and resonance ionization, or a combination thereof.

5. (Currently amended) The method of claim [[3]] 1, wherein the mass spectrometry comprises a step selected from the group consisting of Fourier Transform, ion cyclotron resonance, time of flight analysis with reflection, time of flight analysis without reflection, and quadrupole analysis, or a combination thereof.

6. (Currently amended) The method of claim [[3]] 1, wherein the mass spectrometry comprises matrix-assisted desorption ionization and time of flight analysis.

7. (Currently amended) The method of claim [[3]] 1, wherein the mass spectrometry comprises electrospray ionization and quadrupole analysis.

8. (Currently amended) The method of claim [[3]] 1, wherein two or more molecular weights are determined simultaneously.

9. (Previously presented) The method of claim 1, further comprising the step of enzymatically extending the nucleic acid probes of the target array using the hybridized target nucleic acid as a template to form extended strands prior to the step of determining the molecular weights of the nucleic acids.

10. (Previously presented) The method of claim 9, wherein the extended strands comprise DNA, RNA, PNA or combinations thereof.

11. (Original) The method of claim 9, wherein the step of extending is performed in the presence of chain elongating nucleotides and chain terminating nucleotides.

12. (Original) The method of claim 1, wherein the array comprises nucleic acid probes having at least one mass-modifying functionality.

13. (Original) The method of claim 12, wherein the mass-modifying functionality is coupled to a heterocyclic base, a sugar moiety or a phosphate group.

14. (Original) The method of claim 12, wherein the mass-modifying functionality is a chemical moiety that does not interfere with hydrogen bonding for base-pair formation.

15. (Original) The method of claim 12, wherein the mass-modifying functionality is coupled to a purine at position C2, N3, N7, or C8.

16. (Original) The method of claim 12, wherein the mass-modifying functionality is coupled to a deazapurine at position N7 or N9.

17. (Original) The method of claim 12, wherein the mass-modifying functionality is coupled to a pyrimidine at position C5 or C6.

18. (Original) The method of claim 12, wherein the mass-modifying functionality is selected from the group consisting of F, Cl, Br, I, SiR_3, $Si(CH_3)_3$, $Si(CH_3)_2(C_2H_5)$, $Si(CH_3)(C_2H_5)_2$, $Si(C_2H_5)_3$, $(CH_2)_nCH_3$, $(CH_2)_nNR_2$, CH_2CONR_2, (CH_2)nOH, CH_2F, CHF_2, and CF_3;

wherein n is an integer; and

wherein R is selected from the group consisting of -H, deuterium and alkyls, alkoxys and aryls of 1-6 carbon atoms, polyoxymethylene, monoalkylated polyoxymethylene, polyethylene imine, polyamide, polyester, alkylated silyl, heterooligo/polyaminoacid and polyethylene glycol.

19. (Original) The method of claim 12, wherein the mass-modifying functionality is $-N_3$ or -XR,

wherein X is selected from the group consisting of -O-, -NH-, -NR-, -S-, $-OCO(CH_2)_nCOO-$, $-NHCO(CH_2)_nCOO-$, $-OSO_2O-$, $-OCO(CH_2)_{n-}$, -NHC(0)-, and -C(O)NH-, and n is an integer from 1 to 20; and

wherein R is selected from the group consisting of -H, deuterium and alkyls, alkoxys and aryls of 1-6 carbon atoms, polyoxymethylene, monoalkylated polyoxymethylene, polyethylene imine, polyamide, polyester, alkylated silyl, heterooligo/polyaminoacid and polyethylene glycol.

20. (Original) The method of claim 19, wherein X is -NHC(S)-.

21. (Original) The method of claim 19, wherein X is -NHC(S)NH-.

22. (Original) The method of claim 19, wherein X is $-NC_4O_2H_3S-$.

23. (Original) The method of claim 19, wherein X is $-OCO(CH_2)_nS-$.

24. (Original) The method of claim 23, wherein X is $-OCO(CH_2)S-$.

25. (Original) The method of claim 19, wherein X is -OP(O-alkyl)-.

26. (Original) The method of claim 19, wherein X is -OPO(O-alkyl)-.

27. (Original) The method of claim 12, wherein the mass-modifying functionality is a thiol moiety.

28. (Previously presented) The method of claim 27, wherein the thiol moiety is generated by using Beucage reagent.

29. (Original) The method of claim 12, wherein the mass-modifying functionality is an alkyl moiety.

30. (Original) The method of claim 29, wherein the alkyl moiety is generated by using iodoacetamide.

31. (Previously presented) The method of claim 1, further comprising the step of removing alkali cations.

32. (Previously presented) The method of claim 31, wherein the alkali cations are removed by ion exchange.

33. (Original) The method of claim 32, wherein the ion exchange comprises contacting the nucleic acid with a solution selected from the group consisting of ammonium acetate, ammonium carbonate, diammonium hydrogen citrate, and ammonium tartrate, or combinations thereof.

34. (Previously presented) The method of claim 1, further comprising the step of ligating the hybridized target nucleic acids to the probes.

35. (Original) The method of claim 1, wherein the target nucleic acid is provided from a biological sample.

36. (Original) The method of claim 35, wherein the biological sample is obtained from a patient.

37. (Original) The method of claim 1, wherein the target nucleic acid is provided from a recombinant source.

38. (Original) The method of claim 1, where the target nucleic acid is between about 10 to about 1,000 nucleotides in length.

39. (Original) The method of claim 1, where the nucleic acid fragments are between about 10 to about 1,000 nucleotides in length.

40. (Original) The method of claim 1, wherein each sequence of the nucleic acid fragments is homologous with at least a portion of the sequence of the target nucleic acid.

41. (Original) The method of claim 1, wherein each sequence of the set of nucleic acid fragments is complementary with at least a portion of the sequence of the target nucleic acid.

42. (Original) The method of claim 1, comprising the step of dephosphorylating the nucleic acid fragments by treatment with a phosphatase prior to hybridization.

43. (Original) The method of claim 1, wherein the fragments are provided by enzymatic digestion of the target nucleic acid.

44. (Previously presented) The method of claim 43, wherein the enzymatic digestion is carried out by a nuclease.

45. (Original) The method of claim 1, wherein the nucleic acid fragments are provided by physically cleaving the target nucleic acid.

46. (Original) The method of claim 1, wherein the nucleic acid fragments are provided by enzymatic polymerization, wherein the target nucleic acid is a template.

47. (Original) The method of claim 46, wherein the enzymatic polymerization is a nucleic acid amplification process selected from the group consisting of strand displacement amplification, ligase chain reaction, Qβ replicase amplification, 3SR amplification, and polymerase chain reaction.

48. (Original) The method of claim 46, wherein the enzymatic polymerization is carried out in the presence of chain elongating nucleotides and chain terminating nucleotides.

49. (Original) The method of claim 1, wherein the nucleic acid fragments are provided by synthesizing a complementary copy of the target sequence.

50. (Cancelled).

51. (Original) The method of claim 1, wherein the nucleic acid fragments comprise DNA, RNA, PNA or combinations thereof.

52. (Original) The method of claim 1, wherein the target nucleic acid comprises DNA, RNA, PNA or modifications of combinations thereof.

53. (Original) The method of claim 1, wherein the fragments of nucleic acids comprise greater than about 10^4 different members and each member is between about 10 to about 1,000 nucleotides in length.

54. (Original) The method of claim 1, wherein the probes are single-stranded.

Claims 55 - 57 (Cancelled).

58. (Original) The method of claim 1, wherein the probes are about 10 to about 1,000 nucleotides in length.

59. (Original) The method of claim 1, wherein the probes are about 15 to about 200 nucleotides in length.

60. (Original) The method of claim 1, wherein the probes are about 10 to 50 nucleotides in length.

Claims 61 and 62 (Cancelled).

63. (Original) The method of claim 1, wherein the variable region is about 4 to about 20 nucleotides in length.

64. (Original) The method of claim 1, wherein the array of nucleic acid probes is attached to a solid support.

65. (Original) The method of claim 64, wherein the solid support is selected from the group consisting of plates, beads, microbeads, whiskers, combs, hybridization chips, membranes, single crystals, ceramics, and self-assembling monolayers.

66. (Original) The method of claim 64, wherein the probes are conjugated with biotin or a biotin derivative and wherein the solid support is conjugated with avidin, streptavidin or a derivative thereof.

67. (Previously presented) The method of claim 64, wherein each probe is attached to the solid support by a bond selected from the group consisting of a covalent bond, an electrostatic bond, a hydrogen bond, a cleavable bond, a photocleavable bond, a disulfide bond, a peptide bond, a diester bond, a selectively releasable bond and combinations thereof.

68. (Original) The method of claim 67, wherein the cleavable bond is cleaved by a cleaving agent selected from the group consisting of heat, an enzyme, a chemical agent, and electromagnetic radiation, or a combination thereof.

69. (Original) The method of claim 68, wherein the chemical agent is selected from the group consisting of reducing agents, oxidizing agents, and hydrolyzing agents, or a combination thereof

70. (Original) The method of claim 68, wherein the electromagnetic radiation is selected from the group consisting of visible radiation, ultraviolet radiation, and infrared radiation.

71. (Previously presented) The method of claim 67, wherein the bond is a selectively releasable bond and comprises 4, 4'-dimethoxytrityl or a derivative thereof.

72. (Original) The method of claim 71, wherein the derivative is selected from the group consisting of 3 or 4 [bis-(4-methoxyphenyl)]-methyl-benzoic acid, N-succinimidyl-3 or 4 [bis-(4-methoxyphenyl)]-methyl-benzoic acid, N-succinimidyl-3 or 4 [bis-(4- methoxyphenyl)]-hydroxymethyl-benzoic acid, N-succinimidyl-3 or 4 [bis-(4- methoxyphenyl)]-chloromethyl-benzoic acid and salts thereof.

73. (Original) The method of claim 64, comprising a spacer between each probe and the solid support.

74. (Original) The method of claim 73, wherein the spacer is selected from the group consisting of oligopeptides, oligonucleotides, oligopolyamides, oligoethyleneglycerol, oligoacrylamides, and alkyl chains of between about 6 to about 20 carbon atoms, or combinations thereof

75. (Previously presented) The method of claim 64, wherein the solid support comprises a matrix chemical that facilitates volatilization of nucleic acids for molecular weight determination.

76. (Original) The method of claim 1, wherein the nucleic acid probes comprise DNA, RNA, PNA, or combinations thereof

Claims 77– 127 (Cancelled).

128. (Previously presented) The method of claim 1, wherein the probes comprise a double-stranded portion and a single-stranded portion.

Claims 129-144 (Cancelled)

145 (Previously presented) The method of claim 1, wherein:

each probe comprises a double-stranded portion and a single-stranded portion; and either or both the single-stranded region and the double-stranded region includes a constant sequence as a point of reference for subsequent analysis.

Claims 146-147 (Cancelled).

148. (New) The method of claim 1, wherein sequencing redundancy is reduced by saturating the array with phosphatased double-stranded targets.

149. (New) The method of claim 1, wherein sequencing redundancy is reduced by monitoring the array by confocal microscopy after elongation reactions.